



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2019-N-3500]

Fit for Use Pilot Program Invitation for the Clinical Data Interchange Standards Consortium for Standard for Exchange of Nonclinical Data Implementation Guide: Version 3.1

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing that it intends to conduct a Fit for Use (FFU) pilot program to test the processing and analysis of nonclinical study data provided electronically for the Clinical Data Interchange Standards Consortium (CDISC) for Standard for Exchange of Nonclinical Data (SEND) Implementation Guide (IG): Version 3.1 (SEND 3.1). The Agency's Center for Drug Evaluation and Research (CDER) will test the processing and analysis of nonclinical study data provided electronically in SEND 3.1 format. FDA is inviting individual firms that wish to participate in this pilot program to submit participation requests via email or in writing.

DATES: To be considered for participation in the pilot program, submit electronic or written requests by [INSERT 30 DAYS FROM PUBLICATION IN THE *Federal Register*]. See the ADDRESSES section for participation request instructions.

ADDRESSES: Submit electronic requests to participate in the pilot and comments regarding this pilot project to <https://www.regulations.gov>. Submit written requests to participate in the pilot and comments regarding the pilot to Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The

<https://www.regulations.gov> electronic filing system will accept comments until 11:59 p.m. Eastern Time by [INSERT 30 DAYS FROM PUBLICATION IN THE *Federal Register*]. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

### *Electronic Submissions*

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

### *Written/Paper Submissions*

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked, and identified, as confidential, if submitted as detailed in “Instructions.”

*Instructions:* All submissions received must include the Docket No. FDA-2019-N-3500 for “Fit for Use Pilot Program Invitation for the Clinical Data Interchange Standards Consortium for Standard for Exchange of Nonclinical Data Implementation Guide: Version 3.1.” Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover

sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

*Docket:* For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Isaac Chang, Office of Computational Science, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave. Silver Spring, MD 20993, 240-402-7501, [PRASStaff@fda.hhs.gov](mailto:PRASStaff@fda.hhs.gov).

#### SUPPLEMENTARY INFORMATION:

##### I. Background

Data standards help FDA receive, process, review, and archive submission data more efficiently and effectively. Study data standards describe a standard way to exchange clinical and nonclinical research data between computer systems. These standards provide a consistent general framework for organizing study data, including templates for datasets, standard names for variables, and standard ways of doing calculations with common variables. Study data

standards are required for study data submitted to FDA's Center for Drug Evaluation and Research (CDER) per the published guidance<sup>1</sup>.

CDISC is an open, multidisciplinary, nonprofit organization that has established worldwide industry standards to support the electronic acquisition and submission of study data and metadata for medical and biopharmaceutical product development.<sup>2</sup> CDISC is currently facilitating and testing the extension of the SEND 3.1 standard for nonclinical toxicology data.

CDER completed a pilot project evaluating SEND 3.0 using SEND-formatted sample toxicology datasets. Phase 1 of the pilot supported the development of a SEND Implementation Guide (SENDIG) describing the process for formatting data from single and repeat-dose animal toxicity and carcinogenicity studies for submission purposes. During Phase 2 of the pilot, CDER evaluated submission of SEND formatted datasets and evaluated data validation and analysis tools capabilities. The outcomes of this pilot resulted in improvements to the SENDIG 3.0.<sup>3</sup>

Based on published guidance<sup>4</sup> studies initiated after December 17, 2016, must be submitted with data formatted in accordance with the data standards listed in the FDA Data Standards Catalog for new drug applications (NDAs), biologics license applications (BLAs), and abbreviated new drug applications (ANDAs). For investigational new drug applications (INDs), the requirement<sup>5</sup> applies to studies initiated after December 17, 2017. SEND 3.1 is included in the Data Standards Catalog, and the submission of SEND nonclinical datasets is expected to continue to increase in the future. This pilot will evaluate the compliance of sample SEND 3.1

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<sup>1</sup> See the guidance Providing Regulatory Submissions in Electronic Format - Standardized Study Data: Guidance for Industry (PDF - 136KB) (Dec. 2014) at <https://www.fda.gov/media/82716/download>

<sup>2</sup> See the CDISC website at <http://www.cdisc.org>.

<sup>3</sup> The updated guide can be found at <http://www.cdisc.org/>. FDA has verified the website address, but the Agency is not responsible for any subsequent changes to the website address after this document publishes in the *Federal Register*.

<sup>4</sup> See the Technical Rejection Criteria for Study Data at <https://www.fda.gov/media/100743/download>

<sup>5</sup> See footnote 4

datasets submitted to CDER. As part of this evaluation and in anticipation of FDA receiving datasets for regulatory review, the CDISC SEND team, in collaboration with CDER and available pilot participants, will update the SENDIG 3.1 as needed to include specific data elements and terms.

## II. Project Participation

CDER is seeking a maximum of five participants in this pilot. The Center will use its discretion in choosing participants based on the completeness of the submission per the guidelines below. CDER requests participants to submit a nonclinical study package containing the following materials:

- SEND 3.1 datasets<sup>6</sup>
- Sample related study report<sup>7</sup> (PDF format)
- Nonclinical Study Data Reviewers Guide<sup>8</sup>
- Define.xml (v2.0)<sup>9</sup>
- Sample standardized study protocol

CDER will prioritize nonclinical packages that highlight the most significant changes from SENDIG 3.0 to SENDIG 3.1 and therefore, the studies that meet as many of the following criteria as possible:

1. Toxicology studies with safety pharmacology data that demonstrate appropriate use of:
  - a. Continuous data typically included in these safety pharmacology studies:

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<sup>6</sup> See the FDA Study Data Resources web page, available at <https://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/default.htm>.

<sup>7</sup> See Footnote 6

<sup>8</sup> See the PhUSE Wiki web page, available at [https://www.phusewiki.org/wiki/index.php?title=Nonclinical\\_Study\\_Data\\_Reviewers\\_Guide](https://www.phusewiki.org/wiki/index.php?title=Nonclinical_Study_Data_Reviewers_Guide).

<sup>9</sup> See Footnote 6

- i) Cardiovascular data represented in the Electrocardiogram (ECG) Test Results Domain, Electrocardiogram Domain (EG), and the Cardiovascular Test Results Domain (CV).
- ii) Respiratory data in the Respiratory Test Results Domain (RE).
- b. Timing variables for Planned Start of Assessment Interval (--STINT), and Planned End of Assessment Interval (--ENINT) (in the use of timing variables in the EG domain).
- c. Unscheduled Flag, (--USCHFL) variable.
- d. Nominal Study Day for Tabulations, (--NOMDY), Label for Nominal Study Day, (--NOMLBL) variable to group and label data for reporting purposes.
- e. Study data from a study or studies using the Latin Square design.
- 2. Toxicology studies including Pharmacokinetic Concentrations Domain (PC) and Pharmacokinetics Parameters Domain (PP) domains.
- 3. Toxicology studies with study data using controlled terminology (version 2018-03-30 or later) for:
  - a. Severity.
  - b. Non-neoplasm (NONNEO) using codelist NONNEO and Microscopic Domain (MI).

Please indicate in your request for participation the extent to which your submission will meet the above listed criteria.

This pilot is intended to inform on the readiness of the SEND 3.1 standard and support improvements to the SENDIG 3.1 that will benefit FDA and submitters. Pilot participants commit to publicly share lessons learned with the CDISC SEND team to ensure that the CDISC

SEND standard is improved for the community. Participants may redact any sensitive information as needed to enable sharing FDA feedback with the CDISC SEND team.

### III. Requests for Participation

Requests to participate in the SENDIG 3.1 FFU pilot are to be identified with the docket number found in brackets in the heading of this document. Interested persons should include the following information in the request: contact name, contact phone number, email address, name of the sponsor, address, and license number, as well as the description of criteria met, addressing each of the items in the II. Project Participation section.

Once requests for participation are received, CDER will contact interested sponsors to discuss the pilot project and clarify requirements and expectations. The elapsed time duration of the pilot is expected to be approximately 6 months but may be extended as needed.

Dated: August 14, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

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